Exhibit C

UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

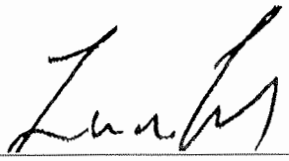
IN RE: ETHICON, INC. **PELVIC REPAIR SYSTEM** **PRODUCTS LIABILITY LITIGATION**	**Master File No. 2:12-MD-02327** **MDL No. 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**

DEFENSE EXPERT GENERAL REPORT

of Lawrence Lind, M.D.:

TVT, TVT-O, TVT Exact and TVT Abbrevo

Prepared by:



Lawrence Lind, M.D.

June 24, 2019

I. Background, Qualifications and Experience

I am the co-chief of the Division of Urogynecology and Pelvic Reconstructive Surgery at North Shore University Hospital and Long Island Jewish Medical Center and Medical Director of the Sharon Joyce Schlanger Center for Women's Care. I am a member of the Quality Assurance Committee of North Shore University Hospital and also Associate Professor in Obstetrics and Gynecology at Northwell Health—Hofstra University School of Medicine. I am also on the review board of the scientific journals Obstetrics & Gynecology and International Urogynecology.

I am a member of the American Urogynecologic Society, a Fellow of the American College of Obstetrics & Gynecology and a Fellow of the American College of Surgeons. I am Board certified in Obstetrics and Gynecology with subspecialty Board certification in Female Pelvic Medicine and Reconstructive Surgery. I attended medical school and residency in Obstetrics and Gynecology at Cornell University Medical College, and I completed a fellowship in Urogynecology and Pelvic Reconstructive Surgery at UCLA Medical Center.

I have authored or co-authored numerous articles in the peer-reviewed scientific literature and book chapters in the field of urogynecology. I have presented abstracts and posters at numerous meetings of professional medical societies, including AUGS, SGS and ACOG. I have taught professional education for Ethicon and served on the speaker's bureau of Astella.

I am presently a senior faculty in a Board Certified Fellowship Training Program in Female Pelvic Medicine and Reconstructive Surgery. The designation as a certified fellowship requires the highest combination of level of clinical skills, teaching and research. I have extensive experience with advisement of companies regarding risks of surgical products for prolapse and incontinence. I have served on design, testing and development teams for sling

products with Boston Scientific and Caldera Medical. I was one of the original designers of the present Capio product, Boston Scientific. Prior to being retained by Boston Scientific I was a principal designer with the Laurus corporation which produced the instrument now called Capio. In advising the Laurus Corporation as well as Boston Scientific, I routinely updated the companies on risks and benefits of the device, information necessary for the physician, information to be included in the IFU and design changes to potentially improve efficacy or reduce risks. I have recently provided design testing of potential new sling products for Caldera medical with a major portion of that advisement involving discussion of the various risks of the procedure and of physician education monographs and company produced materials. I am experienced in both "traditional" surgical procedures to treat stress urinary incontinence, including Burch colposuspension, and placement of mesh midurethral slings. I have used TVT since approximately 2000 and have used TVT Exact since 2010. I also have implanted other mesh midurethral slings including TVT-O and other manufacturers' slings. I have implanted about 3,000 midurethral slings in total, including but not limited to TVT, TVT-O, TVT Exact and TVT Abbrevo. I am referred sling complication cases by other surgeons in the New York metropolitan area. I have trained 225 residents and 10 fellows on the use of midurethral slings. I have extensive experience in treating patients with all urogynecological complaints including dyspareunia, urinary retention and urinary incontinence, and chronic pelvic pain. My *curriculum vitae* is attached.

II. Materials reviewed

I hold the opinions set forth in this report to a reasonable degree of medical and scientific certainty and probability. My opinions and conclusions are based on the practice of evidence-based medicine. I base my opinions on my clinical experience as a practicing urogynecologist;

the peer-reviewed scientific literature, and in particular the systematic reviews and meta-analyses of that literature; the position statements and practice bulletins published by major urogynecologic, gynecologic and urologic medical societies; my analysis of the Ethicon Instructions for Use and professional education content for implanters of TVT, TVT-O, TVT Exact and TVT Abbrevo; and Ethicon's patient brochures; my participation in professional medical society conferences and events; discussions with peers; and my education and training. My opinions are also based on my review of deposition testimony and exhibits, expert reports and materials those reports cite to, and materials published by the FDA. A complete list of the materials I have reviewed is attached to this report and will be supplemented as I review additional materials.

III. Fees and Testimonial History

My fees for serving as an expert in this matter are $500 per hour for report writing, review and consultation. For deposition or court testimony, my fee is $7,500/4,500 for a full day or half day, respectively. As of the writing of this report, I have not yet provided expert testimony in the Ethicon pelvic mesh litigation.

IV. Opinions

A. Stress Urinary Incontinence—Defined

Urinary incontinence (UI) is the unintentional leakage of urine, and subtypes of UI are stress urinary incontinence (SUI), urge urinary incontinence (UUI) and mixed incontinence (MUI), which is a combination of SUI and UUI. The physiologic causes of SUI and UUI are discrete. Treatment modalities differ for SUI and UUI, and a woman who suffers from MUI may need to treat both types of incontinence to achieve continence.

Stress urinary incontinence is the involuntary leakage of urine due to increased abdominal pressure resulting from activities such as coughing, laughing, sneezing, lifting or postural changes. The etiology is multifactorial and includes pregnancy and childbirth, pelvic surgery, disorders of collagen structure and metabolism and ageing. Most patients with SUI have urethral hypermobility or intrinsic sphincter deficiency (ISD) or a combination of both. SUI is the most common form of incontinence and peak prevalence occurs at menopause. Urge incontinence is the involuntary leakage of urine immediately preceded or accompanied by the sensation of urinary urgency. It can be due to such causes as uterovaginal prolapse, atrophic changes, voiding problems, chronic cystitis, recurrent urinary tract infections (UTIs), certain other medical conditions such as neurological conditions, and drug therapies. Ultimately the cause often is detrusor muscle over-activity. The prevalence of all types of UI increases with age. (Christofi, Hextall, Which procedure for incontinence? J Br Menopause Soc, 2005 Mar, 11(1):23-27; Kondo, et al, Prevalence of hand washing incontinence in females in comparison with stress and urge incontinence, Neurourol Urodyn 1990, 19:330-1; National Institute for Clinical Excellence, Guidance on the Use of TVT for Stress Incontinence, Technology Appraisal Guidance No. 56, London: NICE, Feb. 2003.)

Investigation is warranted before treatment. Urodynamic studies, which include noninvasive uroflowmetry followed by multichannel filling cystometry, assess physiological variables during bladder storage and emptying, are often performed preoperatively to confirm and characterize the clinical features of stress urinary incontinence or to guide decisions about modifications in treatment. (Nager, et al, A randomized trial of urodynamic testing before stress-incontinence surgery, N Engl J Med 2012, 366:1987-97.)

B. Prevalence, Cost, and Impact on Quality of Life of Urinary Incontinence

Urinary incontinence, whether stress urinary incontinence (SUI), urge urinary incontinence (UUI) or mixed incontinence (MUI), is a common and bothersome condition that significantly impacts women's quality of life. Approximately half of women experience urinary incontinence at some point in their lives, with SUI a contributory or predominant cause in 30% to 80% of these women. One in three women over age 18 will be affected by SUI at some point in her lifetime. Younger women also experience SUI, and may be more likely to suffer SUI when they are active with child care, employment and elder care. The number of women with SUI only (no UUI) has been conservatively estimated as at least 13 million. (Ford, et al, Mid-urethral sling operations for stress urinary incontinence in women, Cochrane Database of Systematic Reviews 2015 Jul, 7:CD006375.doi:10.1002/14651858.CD006375.pub3; Fultz, et al, Burden of stress urinary incontinence for community-dwelling women, Am J Obstet Gynecol 2003, 189(5):1275-82; Burgio, et al, Prevalence, incidence and correlates of urinary incontinence in healthy middle-aged women, J Urol 1991, 146:1255-9; Diokno, et al., Prevalence of urinary incontinence and other urological symptoms in the noninstitutionalized elderly, J Urol 1986, 136:1022-5.)

The total cost of urinary incontinence has been calculated as $19.5 billion in the U.S., with a cost of $14.2 billion for community residents and a cost of $5.3 billion to institutional residents. Direct costs include routine care such as absorbent products and laundry, treatment, and consequence (e.g., UTIs). Indirect costs include lost productivity due to decrease in probability of working or number of hours worked. Intangible costs include pain and suffering. (Hu, et al, Costs of urinary incontinence and overactive bladder in the United States: A comparative study, Urology 2004, 63(3):461-5.)

Studies have shown, as I have seen in my own treatment of patients, that urinary incontinence results in social consequences, negative feelings and embarrassment in 8-74% of cases, and a moderate to severe impact on quality of life in 10% to 22% of patients. Urinary incontinence has been shown to interfere with marital and sexual life in 7.5% to 33% of patients, and severity of UI has been demonstrated to be directly related to a negative quality of life. (Minassian, et al, Urinary incontinence as a worldwide problem, Int J Obstet Gynecol 2003, 82:327-38.)

C. Treatment

i. Non-Surgical Treatment

Conservative treatment of SUI can be helpful but seldom results in cure. Conservative treatment includes physical therapies and anti-incontinence devices such as pessaries. Lifestyle interventions such as weight loss, smoking cessation and dietary modifications can also be helpful. Physical therapy includes pelvic floor muscle training (PFMT), such as Kegel exercises. PFMT may be offered as a first-line conservative therapy for persistent UI symptoms. PFMT has been demonstrated to be more effective than no treatment, a placebo drug or an inactive control for women with SUI, UUI or MUI. There does not appear to be a clear benefit of adding biofeedback to PFMT. However, the efficacy of PFMT in preventing SUI has not been proven, and as with any exercise regime, outcomes depend on patient adherence. Pessaries have been demonstrated to produce a positive effect on women's quality of life but must be removed for cleaning and sometimes for sexual intercourse; associated complications are pain, erosion, discharge, infection, bleeding and ulcers. A recent literature review determined that pessaries have been shown to improve urinary symptoms in 50% of women after two months of use but

that also occult UUI is a common adverse effect of pessary use. (Dumoulin, et al, Conservative management for female urinary incontinence and pelvic organ prolapse review 2013: Summary of the 5th international consultation on incontinence, Neurourol Urodyn 2016, 35:15-20; Berghmans, et al, Conservative treatment of stress urinary incontinence in women: a systematic review of randomized clinical trials, Br J Urol 1998, 82:181-191; Coelho, et al, Female pelvic organ prolapse using pessaries: systematic review, Int Urogynecol J 2016 Dec, 27(12):1797-1803; Kuhn, et al, Sexual and organ function in patients with symptomatic prolapse: are pessaries helpful? Fertil Steril 2009, 91(5):1914-8; Cundiff, et al, The PESSRI study: symptom relief outcomes of a randomized crossover trial of the ring and Gellhorn pessaries, Am J Obstet Gynecol 2007, 196(4):405.e1-8; Komesu, et al, Pelvic floor symptom changes in pessary users, Am J Obstet Gynecol 2007, 197(6):620:e1-6.)

Injectable urethral bulking agents administered transurethrally or periurethrally include paraffin, cartilage, autologous fat, glutaraldehyde cross-linked collagen and vulcanized silicone rubber particles suspended in a non-silicone carrier gel. Data regarding the use of bulking agents are limited, but existing data shows that cure rates are low. While complications are rare and short-lived, only 30-40% of women remain dry three to four years after treatment. (Christofi, Hextall, Which procedure for incontinence? J Br Menopause Soc, 2005 Mar, 11(1):23-27.) Collagen was widely used for decades. The present material used for urethral bulking is 'Macroplastique.' This is an office or ambulatory surgical suite procedure in which the bulking agent is injected into the urethra via a cystoscope. The lumen of the urethra is narrowed by the bulking agent conferring improved resistance to leakage of urine. (Rosenfeld, et al, Macroplastique outcome in women with stress urinary incontinence secondary to intrinsic sphincteric deficiency, Urological Science 2014, DOI: 10.1016/j.urols.2015.02.001.)

ii. History of Surgical Treatment

Surgical treatments for SUI have existed for decades, with the first urethral sling described in the medical literature in the early 20th century. By the 1980s more than 100 surgical procedures for the treatment of genuine stress incontinence had been developed, with a focus on elevating the bladder neck, including an anterior vaginal repair (developed in the 19th century), the Kelly plication (introduced in 1913), the Marshall-Marchetti-Krantz (MMK) repair (1949), the Pereyra needle suspension procedure (1959) with numerous variations thereof, and the Burch colposuspension (1968). These earlier surgeries were based on theories such as the angle theory of incontinence. The MMK has fallen out of favor due to the serious complication of osteitis pubis, which occurred at a rate of 5 to 10 percent, and declining success rates over time. Anterior repair, Kelly plication and Pereyra-type procedures are now considered substandard in treating SUI due to high recurrence rates. (Stanton, Stress incontinence: Why and how operations work, Urol Clin North Am 1985 May, 12(2):279-84; Galloway, et al, The complications of colposuspension, Br J Urology 1987, 60:122-124; Rapp, Kobashi, The evolution of midurethral slings, Nat Clin Pract Urol 2008 Apr, 5(4)194-201; Bent, Stress urinary incontinence, Te Linde's Operative Gynecology, 10th ed., Lippincott Williams & Wilkins, 2007, pp. 942-58.)

In my specialty training (1990-1996), all of the above procedures were advocated. The evidence regarding short-term and long-term success and complications associated with these procedures was variable. (Bergman, et al, Comparison of three different surgical procedures for genuine stress incontinence: prospective randomized study, Am J Obstet Gynecol, 1989 May, 160:1102-1106.) Consensus was lacking, and consequently, surgeon choice of procedure was highly variable and depended on the background of the surgeon and the mentor from who they

learned. Patients with stress incontinence could be offered any one of ten different procedures, depending not always on scientific data, which was lacking, but on how and where their surgeon trained.

It is perhaps the most significant, research-based and clinical volume-based change in the last several decades that a problem initially treated many different ways is now treated initially the same way by almost all clinical experts. That change, in the late 1990s, was due to the TVT. TVT was vigorously studied by experts in case series and randomized controlled trials. Based on the safety and efficacy data and ease of performance, TVT became the most commonly performed initial treatment for stress incontinence. In the setting of increasingly academic and research-based specialties (Urogynecology, Female Urology, Female Pelvic Medicine & Reconstructive Surgery), TVT equaled or outperformed the "traditional" procedures that preceded it. TVT did not quietly displace a solitary dominant procedure; rather, the practitioners in our field proved through rigorous scientific analysis that TVT was superior to many existing alternative options for stress incontinence, and that it was the new gold standard. I cannot think of another condition for which surgical treatment has transformed so completely.

a. Use of Grafts in Suburethral Slings to Treat SUI

Suburethral sling placement to treat SUI, with the use of gracilis muscle, was introduced as early as 1907, and other harvest sites were identified over the subsequent 35 years. Today, fascial slings are performed using fascia lata, harvested from the leg using a stripper, or rectus fascia, harvested from the abdomen. Because of additional operative time and morbidity to harvest autologous materials, biomaterials such as cadaveric allografts or porcine or bovine xenografts have been used, although these materials carry heightened risk of infection and rejection. (Stanton 1985; Bent 2007.) In addition, all of the procedures that involve use of

autologous graft require surgery at two locations on the patient adding to the surgical complexity and level of invasiveness. As a result, surgeons have turned to synthetic alternatives that did not have these disadvantages of biological grafts.

The use of a synthetic sling to treat SUI was first described in the medical literature in the 1960s. Other meshes used in slings to treat SUI have included nylon, Mersilene (polyester) and Gore-tex (PTFE), and use of these slings was reported on in the scientific literature in the 1960s, 70s, 80s and 90s. (Williams, Te Linde, The sling operation for urinary incontinence using Mersilene ribbon, Obstet Gynecol 1962 Feb, 19(2):241-5; Moir, The gauze-hammock operation (a modified Aldridge-sling procedure), J Obstet Gynaecol Br Common 1968, 75:1-9; Nichols, The Mersilene mesh gauze-hammock for severe urinary stress incontinence, Obstet Gynecol 1973 Jan, 41(1): 88-93; Spencer, et al, The gauze hammock operation in the treatment of persistent stress incontinence, J Obstet Gynaecol Common 1972, 79:666-9; Bryans, Marlex gauze hammock sling operation with Cooper's ligament attachment in the management of recurrent urinary stress incontinence, Am J Obstet Gynecol 1979, 133:292-4; Kersey, The gauze hammock sling operation in the treatment of stress incontinence, Br J Obstet Gynaecol 1983 Oct, 90:945-9; Young, et al, The Mersilene mesh suburethral sling: A clinical and urodynamic evaluation, Am J Obstet Gynecol 1995 Dec, 1719-1726.)

Amid and colleagues analyzed the biocompatibility of Gore-Tex, Teflon, Surgipro, Marlex, Prolene and Mersilene meshes in order to report on the requirements of biomaterials and principals of their surgical application. They reported that monofilament polypropylene mesh is superior to other available synthetic materials as it is inert, resists infection and sinus tract formation, has rapid fibrinous fixation and becomes completely incorporated into the host tissue. Macroporous biomaterials with pore sizes larger than 75 microns, such as monofilament

polypropylene mesh, do not promote or harbor infection, whereas microporous biomaterials with pores smaller than 10 microns (such as Gore-Tex, Mersilene, Surgipro and Teflon) can promote or harbor infections. Complete incorporation of the mesh with the host tissue is important for a solid repair, and the degree of host tissue infiltration depends on pore tissue. Proper incorporation requires a pore size of 75 to 100 microns. (Amid, et al, Biomaterials for abdominal wall hernia surgery and principles of their applications, Langenbecks Arch Chir 1994, 379: 168-71.)

b. Development of the TVT

From the 1950s through the 1980s, clinicians presented a series of discoveries and ideas that would lead in the 1990s to Ulmsten and Petros's integral theory. This theory implied a paradigm shift in the understanding of the mechanism of stress incontinence. Ulmsten put the theory into practice by developing a new minimally invasive, ambulatory, standardized surgical procedure, the TVT, which was launched in Europe in 1997 and in the U.S. in 1998. Ulmsten and Petros developed the TVT to provide support at the midurethra that prevents urine leakage. Several modifications of the procedure were trialed, including the use of Mersilene and Gore-tex tapes, but Prolene was ultimately chosen because it was the material best tolerated by patients. Novel aspects of the TVT included placement at the midurethra and use of a "tension-free" placement, rather than directly against the urethra, which minimized direct urethral pressure and therefore risk of urinary obstruction. TVT revolutionized treatment of SUI. (Nilsson, Creating a gold standard surgical procedure: the development and implementation of TVT, Int Urogynecol J 2015 Apr, 26(4):467-9; Petros, Creating a gold standard surgical device: scientific discoveries leading to TVT and beyond, Int Urogynecol J 2015 Apr, 26(4):471-6; Rapp, Kobashi 2008.)

The TVT was designed to be safe and efficacious. The monofilament, macroporous polypropylene Prolene mesh was selected as it was the most biocompatible material. The mesh also stays in place after removal of the plastic sheath over the mesh. The plastic sheath facilitates placement of the sling into the correct position, minimizes tissue trauma and prevents contamination of the sling during implantation. The design of the needles or trocars allow the sling to be placed in the correct anatomical position via small incisions and surgical pathways. The minimally invasive nature of the surgery results in minimal surgical trauma, allows the procedure to be performed under local anesthesia if desired, and results in an operation time that is less than half of the time required for a Burch procedure and even shorter than an autologous pubovaginal sling procedure. (Ulmsten, et al, An ambulatory surgical procedure under local anesthesia for treatment of female urinary incontinence, Int Urogynecol J 1996, 7:81-86; Demirci, Yucel, Comparison of pubovaginal sling and Burch colposuspension procedures in type I/II genuine stress incontinence, Arch Gynecol Obstet 2001, 265:190-4.)

Ethicon's TVT Obturator (TVT-O) midurethral sling was introduced in 2004. The TVT-O midurethral sling is placed via the obturator approach. The device includes a Prolene mesh that is identical to the mesh in retropubic TVT, as well as helical passers and atraumatic winged guides. The TVT-O is placed via an "inside-out" technique (as opposed to "outside-in") through the obturator foramens. The TVT-O was developed by Professor Jean de Leval with the goal of reducing the risk of certain complications of TVT, including injury to the bladder and urethra, particularly in high-risk patients. (De Leval, J., Novel surgical technique for the treatment of female stress urinary incontinence: Transobturator vaginal tape inside-out, Eur Urol, 44:724-730, 2003; Reisenauer, C, et al, Transobturator vaginal tape inside-out: A minimally invasive treatment of stress urinary incontinence: Surgical procedure and anatomical conditions, Eur J

Obstet Gynecol Reprod Biol, 127:123-129, 2006.) The helical passer is designed to assure that the device is directed away from the obturator neurovascular bundle. (Rogers, R, et al, Anatomic considerations for the TVT-Obturator approach for the correction of female stress urinary incontinence, ICS, IUGA Abstract No 155, 2004.) Hyperflexion of the hips is necessary for correct placement of the TVT-O. (TVT Obturator IFU ©2003; Hubka, P, et al, Anatomical study of position of the TVT-O to the obturator nerve influenced by the position of the legs during the procedure: based upon findings at formalin-embalmed and fresh-frozen bodies, Arch Gynecol Obstet, 294:901-905, 2011.)

The TVT Exact, launched in 2010, maintains the key components and concepts of the TVT but features a single-use ergonomically designed handle and trocars that measure 3-mm instead of a stainless steel handle and 5-mm trocars. The mesh material is identical and the anatomic pathway is identical to the TVT. The trocar is disposable instead of reusable and is 2 mm smaller than the trocars in the TVT. (Thubert, et al, Bladder injury and success rates following retropubic midurethral sling: TVT Exact vs. TVT, Eur J Obstet Gynecol Reprod Biol 2016 Mar, 198:78-83.)

The TVT Abbrevo was also launched in 2010 and includes a 12-cm–long Prolene mesh, helical passers, atraumatic winged guide and placement loop. TVT Abbrevo avoids perforation of the obturator membrane with the scissors and guide, which reduces the depth of latcral dissection and maximizes securing of the mesh within the obturator muscular and aponeurotic structures. (Waltregny, D., de Leval, J., New surgical technique for treatment of stress urinary incontinence TVT Abbrevo: From development to clinical experience, Surgical Technique International XXII, Gynecology, 2012.)

TVT, TVT-O, TVT Exact and TVT Abbrevo are suitable for women having their first operation to prevent incontinence as well as women who previously had an unsuccessful SUI surgery. (Ong, HL, et al, Repeat retropubic suburethral sling procecure is effective for recurrent female stress urinary incontinence, Lower Urinary Tract Symptoms, 11:O89-O92, 2019; Kavanagh, A., et al., Management of patients with stress urinary incontinence after failed midurethral sling, Can Urol Assoc J, 2017 Jun; 11(6Suppl2): S143–S146.) Polypropylene midurethral slings including TVT, TVT-O, TVT Exact and TVT Abbrevo are appropriate for most female patients with SUI. (Ford 2015; Dmochowski, et al, Female stress urinary incontinence update panel of the American Urological Association Education and Research, Inc. Update of AUA guideline on the surgical management of female stress urinary incontinence, J Urol 2010, 183(5): 1906-1914; SUFU, Position statement on mesh midurethral slings for stress urinary incontinence, http://www.sufuorg.com/docs/guidelines/AUGS-SUFU-MUS-Position-Statement-APPROVED-1-3-2014.aspx, 2014.)

D. Complications

No surgery is risk-free. The role of informed consent is for surgeons to appropriately advise patients of potential benefits and harms of a proposed surgery so that the patient, with her surgeon, can proceed after evaluating both. Evaluation of risk factors for complications should be part of the informed consent process. Potential benefits and potential risks should be weighed and balanced against a specific patient's goals and desires. Surgeons should also advise their patients of their own success and complication rates as well as rates that are published in the peer-reviewed literature. In our practice, the complication rates with TVT, TVT-O, TVT Exact and TVT Abbrevo are infrequent, and almost without exception, complications can be resolved with the patient remaining continent and pain free.

The potential complications of TVT, TVT-O, TVT Exact and TVT Abbrevo constitute the same set of potential complications of all non-mesh SUI surgeries. They are commonly known to experienced pelvic surgeons. They include acute and/or chronic pain; acute and/or chronic pain with intercourse; vaginal scarring; infection; urinary problems including frequency, urgency, dysuria, retention, obstruction and incontinence; organ or nerve damage; bleeding; wound complications; inflammation; fistula formation; neuromuscular problems including in pelvic floor muscles, lower extremities and/or the abdominal area; one or more surgeries to treat an adverse event; recurrence or failure; foreign body response; erosion, exposure and extrusion; and contraction or shrinkage of tissues. These complications are also risks of non-mesh SUI surgeries as noted in the medical literature. (Stanton 1985; Gomelsky 1987; Iglesia, et al, Int Urogynecol J 1997, 8:105-115; Albo 2007; Schimpf 2014; Ford 2015.)

i. Exposure

The risk of exposure or erosion of sling material has been known since long before the advent of TVT. (Stanton 1985.) Mesh exposure with midurethral slings including TVT has been reported in the medical literature for many years and it is a complication commonly known to experienced pelvic surgeons. (Dietz, et al, Mechanical properties of urogynecologic implant materials, Int Urogynecol J 2003, 14:239-243; Choe, The Use of Synthetic Materials in Pubovaginal Sling, Bladder Disease: Research Concepts and Clinical Applications, Plenum Pub., 2003, Ch. 33, pp. 481-492; Abdel-Fattah, et al, Pelvicol Pubovaginal Sling versus Tension-Free Vaginal Tape for Treatment of Urodynamic Stress Incontinence: A Prospective Randomized Three-Year Follow-Up Study, Eur Urol 2004, 629-635; Abdel-Fattah, et al, How common are tape erosions? A comparison of two versions of the transobturator tension-free vaginal tape

procedure, Brit J Urol 2006, 98:594-598; Achtari, et al, Risk factors for mesh erosion after transvaginal surgery using polypropylene (Atrium) or composite polypropylene/polyglactin 910 (Vypro II) mesh, Int Urogynecol J 2005, 16:389-394.)

Mesh exposure after a midurethral sling procedure occurs in only 1 to 2% of cases and is usually successfully managed conservatively. Asymptomatic exposures can be managed expectantly, and re-epithelialization can occur. Small symptomatic exposures that produce spotting or bleeding, discharge or pain can be treated with a trial of vaginal estrogen for 6 to 12 weeks. Expectant management or topical estrogen therapy for vaginal mesh extrusion has been reported to be successful in 37% to 42% of patients. If this is not successful, surgical excision is often an ambulatory procedure well tolerated by most patients. Excision of the entire mesh is usually not necessary, and mesh removal surgery should not be performed unless there is a specific therapeutic indication.

In my experience, mesh exposure typically has one of several benign courses: most often it is sub-clinical in that the patient has no clinical or quality concerns related to the exposure. For some patients, it causes discharge, which usually resolves with time, application of estrogen cream, office-based simple revision, or minor surgical suite revision. Also in my experience, the continence results are usually maintained and overall satisfaction with the procedure remains high.

We see the lowest incidence of mesh exposure with retropubic slings such as TVT. Mesh exposure after any of the TVT slings, TVT, TVT-O, TVT Exact or TVT Abbrevo, is a rare occurrence in our experience, and typically it is asymptomatic. Schimpf's metaanalysis notes a 1.4% summary estimate of incidence of exposure for retropubic slings, 2.2% for obturator slings and 5.4% for pubovaginal slings. (Schimpf 2014.) Usually, exposure appears as a 1-2

centimeter opening of the anterior vaginal incision with the mesh appearing clean, without erythema, pus or discharge. In my experience, this presentation indicates failure of vaginal wall closure site, rather than an active 'extrusion' of the sling. Again, this is addressed simply and successfully.

In our tertiary referral center with more than 20 years seeing referred patients with problems, we have rarely seen infectious, inflammatory, or active appearing extrusion of a retropubic or transobturator sling. The appearance of almost all the exposures we have seen would be described as visual mesh in the absence of erythema, discharge, pus or fever (characteristics which I would associate with active erosion). Nevertheless, infection and inflammatory response and lymphocyte and macrophage reactions with Prolene mesh have been reported in the medical literature for many years and is known to experienced pelvic surgeons. (Choe 2003; Boulanger, et al, Tissue integration and tolerance to meshes used in gynecologic surgery: An experimental study, Eur J Obstet Gynecol Reprod Biol 2006, 125:103-108.) Mesh removal due to defective healing also have been reported for many years. (Wang, et al, A histologic and immunohistochemical analysis of defective vaginal healing after continence taping procedures: A prospective case-controlled pilot study, Am J Obstet Gynecol 2004, 191:1868-1874; Wang, et al, Prospective randomized trial of TVT and TOT as primary treatment for female stress urinary incontinence with or without pelvic organ prolapse in Southeast China, Arch Gynecol Obstet 2010, 281:279-286.) A rare patient describes that her partner can feel something during sexual activity. These cases are observed if asymptomatic, or closed simply in the office or ambulatory surgery if the patient has mild symptoms or is simply concerned about the exposure. On occasion, the male partner may feel the mesh, but this also resolves with spontaneous healing over the mesh or minor revision.

Erosion, a term sometimes used where "exposure" is the correct term, means erosion of mesh into an organ, such as the bladder, rectum or bowel. It is a rare complication. Erosion and exposure are also risks of non-mesh SUI surgeries, however, in that autologous fascial slings and suture material used in a Burch colposuspension can erode or become exposed. (Committee Opinion No. 694: Management of mesh and graft complications in gynecologic surgery, Obstet Gynecol 2017 Apr., 129(4):e102-8; Deffieux, et al, Long-term follow-up of persistent vaginal polypropylene mesh exposure for transvaginally placed mesh procedures, Int Urogynecol J 2012, 23:1387-90; Richter, et al, Retropubic versus transobturator midurethral slings for stress incontinence: Urinary Incontinence Treatment Network, N Engl J Med 2010, 362: 2066-76; Kobashi, Govier, Management of vaginal erosion of polypropylene mesh slings, J Urol 2003, 169: 2242-3; Bang, Autologous pubovaginal slings: back to the future or a lost art?, Res Rep Urology 2016, 8:225-231; Albo, Burch colposuspension versus fascial sling to reduce urinary stress incontinence, N Engl J Med 2007, 356(21): 2143-2155; Marks, Goldman, Controversies in the management of mesh-based complications: A urology perspective, Urol Clin N Am 2012, 39:419-28.)

Plaintiffs' experts assert that their opinions regarding negative bio-mechanical changes, degradation, and other negative properties are supported by certain articles.[1] With regard to the hierarchy of scientific research, none of those articles, or expert opinions are meta analysis. None of those articles are randomized control studies. These are the most important and scientifically

[1] Examples include: Clave, H., Polypropylene as a Reinforcement in Pelvic Surgery is Not Inert: Comparative Analysis of 100 Explant, I Urogynecol J, 2010 21:261-270; Klinge, U., et al., Shrinking of Polypropylene Mesh in Vivo: An Experimental Study in Dogs, Eur J Surg 1998,164: 965-969; Klinge, U., Foreign Body reaction to Meshes Used for the Repair of Abdominal Wall Hernias, Eur J Surg 1998, 164:951–960; Klostherhalfen,B., The lightweight and large porous mesh concept for hernia repair, Expert Rev. Med. Devices 2005, 2(1); Klinge, U., et al., Do Multifilament Alloplastic Meshes Increase the Infection Rate? Analysis of the Polymeric Surface, the Bacteria Adherence, and the In Vivo Consequences in a Rat Model, J Biomed Mater Res 2002, 63:765-771; Cobb, W., et al., The Argument for Lightweight Polyropylene Mesh in Hernia Repair, Surgical Innovation 2005, 12(1):T1-T7.

relevant studies which guide safety decisions and usage recommendations by experts and expert societies of pelvic surgery. For the most part, the negative articles are limited to laboratory studies, case reports, and reports of a series of cases on patients who had adverse events. In contrast, the data supporting the use and safety of polpropylene midurethral slings includes several meta-analyses and several randomized studies. Additional studies supporting the use of midurethral slings, and published opinions by all of the authoritative societies which guide safety recommendations ALL support the use of midurethral slings. These agencies include ACOG, AUGS, AUA, ICS, SGS, and SUFU. The re-affirmation (of a positive position on the use of vaginal mesh for surgical treatment of stress incontinence) by 6 societies in a single consensus statement is unprecedented based on my review, and the 7th expert society, IUGA, published their own positive consensus statement on mid–urethral slings. Therefore, all seven specialist boards who oversee quality, education, and research for incontinence surgery have reviewed the available data and unanimously affirmed a positive position on the use of mid–urethral slings. The midurethral sling, as a result, has become the unquestionable "gold standard" for treatment of stress incontinence and required training for all fellows in Board approved fellowship training programs. With regard to the number of positive versus negative articles, there are more than 2,000 articles supporting the use of midurethral slings compared to relatively few negative articles. In summary, I recognize that there are studies which show negative characteristics of polypropylene mesh and slings. The sparsity of those studies and scientific quality of those studies pales in comparison to the expansive and commanding literature supporting the macroporous, monofilament polypropylene mesh midurethral sling.

ii. Urinary retention

Voiding dysfunction can occur after any type of anti-incontinence procedure. Continence at the expense of increased outlet resistance has been well documented for Burch procedures, autologous pubovaginal slings, and older non-mesh SUI surgeries. Voiding dysfunction with midurethral slings has been reported in the medical literature for many years and it is a complication commonly known to experienced pelvic surgeons. (Rechberger, et al, A randomized comparison between monofilament and multifilament tapes for stress urinary incontinence surgery, Int Urogynecol J 2003, 14:432-436; Arunkalaivanan, Barrington, Randomized trial of porcine dermal sling (Pelvicol implant) vs. Tension-free Vaginal Tape (TVT) in the Surgical treatment of stress incontinence: a questionnaire-based study, Int Urogynecol J 2003, 14:17-23; Mazouni, et al, Urinary complications and sexual function after the tension-free vaginal tape procedure, Acta Obstet Gynecol Scand 2004, 83:955-961.)

The TVT procedure was specifically designed to limit the amount of obstruction. (Klutke, et al, Urinary retention after tension-free vaginal tape procedure: incidence and treatment, Urology 2001, 58(5): 697-701; Galloway 1987; Stanton 1985.) Ford's analysis of seven registries found a urinary retention rate for TVT of 1.6%. (Ford 2015.) The rate of urinary dysfunction after transobturator route slings as reported by Ford is even lower, at 0.53%,. Short-term voiding dysfunction after any of the TVT slings is common and is usually self-limited and resolves with expectant management. Etiologies may include periurethral tissue edema, anesthetic effects, opioids, pain or outlet obstruction.

A TVT, TVT-O, TVT Exact or TVT Abbrevo can, however, inadvertently be placed such that it over-corrects and is too tight. For a patient with stress incontinence, her urethra and normal anatomic 'sling' mechanism are too loose or does not tighten enough during exertion.

All incontinence procedures are performed with a goal of increasing the patient's resistance to leakage. While there are several techniques, with any anti-incontinence surgery, the procedure for gauging how snug or how loose the repair should be for each patient, it is not an exact science. After any incontinence procedure, the new anatomy or implant may have too little tension, just the right amount of tension, and or too much tension. Midurethral slings, like every other incontinence procedure that preceded them, can be placed by the surgeon too loose, just right, or too tight. There is a spectrum of outcomes related to tightness which is broad, and this spectrum is common to all incontinence procedures. Thus, the TVT, TVT-O, TVT Exact or TVT Abbrevo as an individual implant is not responsible for retention. As with any anti-incontinence surgery, the midurethral sling is intended to increase resistance to leakage, and for some patients, despite the science and best surgical precision, the sling can inadvertently be placed such that it is too tight for an individual patient. This is an established possibility for which every patient is counseled. It is also an outcome that is easily addressed in the post-operative period. After six weeks, sling release for ongoing urinary retention may be considered. Most patients remain continent after sling release. (ACOG Cttee Op 694; Rardin, et al, Release of tension-free vaginal tape for the treatment of refractory postoperative voiding dysfunction, Obstet Gynecol 2002, 100:898-902.) Schimpf reported a summary estimate of evidence of 2.7% for urinary retention lasting more than six weeks after retropubic MUS including TVT, 2.4% for TVT-O, as well as 7.5% for pubovaginal slings and 7.6% for Burch. (Schimpf, et al, Sling surgery for stress urinary incontinence in women: A systematic review and metaanalysis, Am J Obstet Gynecol 2014, 211:71e1-27.) In our experience, for the 1 to 2% of patients who have retention that does not resolve in a few days to a week or two, re-accessing the sling and releasing it slightly has easily resolved their retention.

iii. Frequency and urgency

All anti-incontinence procedures can be followed by de novo or continued frequency and urgency. The occurrence of de novo detrusor instability or de novo urgency with slings has been reported in the literature since the early years of TVT. (Bidmead, Cardozo, Sling techniques in the treatment of genuine stress incontinence, Brit J Obstet Gynecol 2000, 107(2):147-156; Rackley, et al, Tension-free vaginal tape and percutaneous vaginal tape sling procedures, Techniques in Urology 2001, 7(2):90-100; Bhargava, et al, Rising awareness of the complications of synthetic slings, Curr Opin Urol 2004, 14:317-321; Shah, et al, Broad-based tension-free synthetic sling for stress urinary incontinence: 5-year outcome, J Urology 2005, 170:849-851.) Urgency and frequency may exist prior to SUI surgery but become more prominent after surgery. (Stanton 1985.) Athanasopoulas and colleagues reported a 29.2% complication rate for autologous fascial sling, with postoperative urgency being the most common problem. Albo reported that 27% of pubovaginal sling patients in the SISTEr trial and 20% of the Burch patients were treated for postoperative urge incontinence. (Albo 2007; Athanasopoulos, et al, Efficacy and preoperative prognostic factors of autologous fascia rectus sling for treatment of female stress urinary incontinence, Urology 2011, 78(5):1034-8.) De novo frequency and urgency can also be seen after TVT, TVT-O, TVT Exact and TVT Abbrevo. Ford and colleagues reported that the average rate of de novo urgency/urge urinary incontinence after retropubic slings was 8.35% in the short term, was similar to that in the medium term, and was 8% in the long term. (Ford 2015.) Schimpf reported a summary estimate of evidence of 6.9% for overactive bladder/ urgency after retropubic slings and of 5.3% after transobturator slings. (Schimpf 2014.)

iv. Failure and Recurrence

Failure is a risk of any surgery. The SISTER trial researchers reported that success rates of both Burch and pubovaginal sling declined steadily over their initial two-year follow-up period, and acknowledged that this finding confirmed previous observations. Continence rates in both groups declined further between two and seven years' follow up, with continence rates decreasing from 42% to 13% in the Burch group and from 52% to 27% in the sling group. (Albo 2007; Kjolhede, Ryden, Prognostic factors and long-term results of the Burch colposuspension: a retrospective study, Acta Obstet Gynecol Scand 1994, 73:642-7; Alcalay, et al, Burch colposuspension: a 10-20 year follow up, Br J Obstet Gynaecol 1995, 102:740-5.) Long-term follow-up of TVT have demonstrated an objective cure rate of 91% at 17 years follow-up and a subjective perception of cure or improvement of more than 87%. (Nilsson, et al, Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence, Int Urogynecol J 2013 Aug, 24(8): 1265-9.) Serati and colleagues' ten-year follow up of their multicenter, prospective study of the safety and efficacy of TVT-O (160 of 168 patients available for follow up) showed that TVT-O is a highly effective and safe option for the treatment of SUI. At 10 years after surgery, 155 of 160 patients (97%) declared themselves cured. Similarly, at 10 years follow up, 148 of 160 patients (92%) were objectively cured. No significant deterioration of objective cure rates was observed over time. However, risk factors related to failure of retropubic and transobturator slings include previous anti-incontinence surgery, ageing, presence of UUI or MUI, obesity and diabetes. Risk factors also include urodynamic findings such as low maximum urethral closure pressure, decreased bladder neck mobility, detrusor overactivity and voiding difficulties. (Bing, et al, Clinical risk factors and

urodynamic predictors prior to surgical treatment for stress urinary incontinence: a narrative review, Int Urogynecol J 2015 Feb, 26(2):175-85.)

v. Bladder Perforation

Injury to organs or structures is a risk of all SUI surgeries, as is commonly known to all experienced pelvic surgeons. Perforation of the bladder or blood vessels or other organs specifically with TVT has been reported in the literature for many years. (Levin, et al, Surgical complications and medium-term outcome results of tension-free vaginal tape: A prospective study of 313 consecutive patients, Neurourol Urodyn 2004, 23:7-9; .) Ford and colleagues reported that bladder perforation occurred in 2.7% to 3.9% of retropubic MUS implants as demonstrated in several large registries and in 0.4% of transobturator MUS implants. The reported sequelae for bladder or urethral perforation is usually of short duration. Intraoperative bladder perforation is managed by repeat placement of the mesh and one to three days of bladder drainage and has no long-term consequences. While the incidence of bladder perforation is higher with retropubic MUS than with obturator route MUS, the risks and benefits of retropubic MUS such as TVT and TVT Exact may be balanced against the benefit and risk profile of obturator route MUS. Both retropubic and obturator route MUS have robust safety and efficacy profiles. (Schimpf 2014; Ford 2015; Nager, Midurethral slings: evidence-based medicine vs. the medicolegal system, Am J Obstet Gynecol 2016 June, 214(6):708e1-5.)

In our clinical experience about 2% of patients have a sling trocar introduced into the bladder with placement of a retropubic sling. All were noted at intraoperative cystoscopy, the trocar was re-passed more lateral, and after 3,000 slings, we have never found a mesh within the bladder, nor have we seen a fistula, following this protocol. The rare patient that has a trocar pass intra-luminal in the bladder has had no negative sequelae.

vi. Shrinkage or contraction

Shrinkage or contraction with implantation of mesh is a phenomenon that was well known before the launch of TVT and has been reported in the literature. (Amid, Classification of biomaterials and their related complications in abdominal wall hernia surgery, Hernia 1997, 1:15-21; Deprest, et al, Synthetic and biodegradable prostheses in pelvic floor surgery, International Congress Series 1279, 2005, 387-397.) Shrinkage of the mesh itself has not been demonstrated in the literature, and it is rather the tissues not the mesh that can shrink or contract, consistent with scar tissue generally. (Bayat, A., et al., Skin scarring, Br Med J, 2003 Jan 11; 326(7380): 88–92.) Dietz et al found an increase in mesh length, as opposed to contraction, in their study of 40 women who had had transvaginal mesh placed in the anterior wall. Lo and colleagues evaluated 70 women implanted with TVT at three years post-op and their observations and measurements of the patients' TVTs showed that shrinkage and compromise of the TVT sling does not occur. (Lo, et al, Ultrasound assessment of mid-urethra tape at three-year follow-up after tension-free vaginal tape procedure, Urology 2004 Apr, 63(4):671-5; Lukacz, et al, The effects of the tension-free vaginal tape on proximal urethral position: a prospective, longitudinal evaluation, Int Urogynecol J 2003, 14:179-84; Dietz, et al, Mesh contraction: myth or reality? Am J Obstet Gynecol 2011, 204(2):173.e1-4; Dietz, et al, Does the tension-free vaginal tape stay where you put it? Am J Obstet Gynecol 2003, 188(4):950-3 ("Dietz 2003").)

vii. Pain

Chronic or long-term pain after TVT, TVT-O, TVT Exact or TVT Abbrevo is rare, but it is a risk of all SUI surgeries and is commonly known to experienced pelvic surgeons. (Francis, Jeffcoate, Dyspareunia following vaginal operations, J Obstet Gynaecol Br Common 1961, 1-10;

Stanton 1985; Galloway 1987.) Chronic pain is a risk of any surgery. (Kalkman, CJ, et al, Preoperative prediction of severe postoperative pain, Pain. 2003 Oct; 105(3):415-23.)

Decreased sexual function with any TVT sling, while rare, has been reported in the literature for many years. (Maaita, et al, Sexual function after using tension-free vaginal tape for the surgical treatment of genuine stress incontinence, Brit J Urol 2002, 90:540-543; Kobashi, Govier, Management of vaginal erosion of polypropylene mesh slings, J Urology, 2003 June, 169:2242-2243; Mazouni 2004; Shah, et al, Impact of vaginal surgery for stress urinary incontinence on female sexual function: is the use of polypropylene mesh detrimental? Urology 2005 Feb, 65(2):270-274.) Male partner discomfort during sexual intercourse after midurethral sling also has been reported in the literature for more than a decade. (Brubaker, L., Editorial: partner dyspareunia (hispareunia), Int Urogynecol J Pelvic Floor Dysfunct, 17(4):311, Jun 2006.) Schimpf reported a summary estimate of evidence of 0.0% for dyspareunia after TVT, as well as a 0.06% rate of nerve injury, a 1.5% rate of groin pain, and a 0.62% rate of leg pain after TVT. (Schimpf 2014.) As noted above, pain is also a risk of non-mesh SUI surgeries. A detailed and systematic examination should be done to localize the anatomy involved in the pain and determine how, or if, it is related to the sling. Levator tone and tenderness should be evaluated as a contributing factor. Conservative management of pain may include physical therapy and trigger-point injections. Sling excision may be an option but should not be performed in the absence of a specific therapeutic indication. (ACOG Cttee Op 694.)

Groin pain and leg pain are known and well established risks of transobturator slings. Hyperflexion of the hips, as noted in the IFU, is important for proper placement of TVT-O. (Hubka 2011.) Prolonged groin pain after midurethral sling including transobturator approach slings is infrequently reported. The majority of cases resolve spontaneously without

intervention. Treatment options include injections of steroid/analgesic and physical therapy. (Roth, T., Management of persistent groin pain after transobturator slings, Int Urogynecol J, 18:1371-1373, 2007.) Schimpf and colleagues found a summary estimate of incidence of groin pain after transobturator slings of 6.5% and after retropubic slings of 1.5% and of leg pain after transobturator sling of 16% and after retropubic sling of 0.62%. They also reported a 0.34% summary estimate of incidence of groin pain after pubovaginal sling. (Schimpf 2014.)

Regarding dyspareunia, in our practice, after placing over 3,000 slings, we have had only one patient report dyspareunia a few years after the sling. Given that sexual activity was comfortable after initial recovery, and with our sling patients otherwise having no negative sexual outcomes for more than 3,000 patients, we feel confident that the TVT slings do not have a negative impact on sexual function. In contrast, our observation (although not statistically quantified) is that for many, sexual function is enhanced from a psychological view. Patients report feeling more confident because everyday odor related to leakage is resolved, as is frank leakage with sexual activity. In addition, vaginal and vulvar irritation are resolved with cessation of incontinence and vulvar contamination. The cumulative sexual impact of TVT slings is in fact improvement of sexual function. For the rare patient who does have vaginal or sexual pain after a sling, revision of the sling routinely resolves the issue. Schimpf et al report a summary estimate of incidence of dyspareunia of 0.00% for retropubic slings, 0.16% for obturator slings and 0.99% for pubovaginal slings. (Schimpf 2014.) Dyspareunia also has been documented in the peer reviewed medical literature as a complication of Burch colposuspension. (Weber, A., et al., Sexual function and vaginal anatomy in women before and after surgery for pelvic organ prolapse and urinary incontinence, Am J Obstet Gynecol, 182(6): 1610-1615, 2000.)

Regarding nerve pain, again with a cohort of more than 3,000 cases, the only nerve pain we have seen is 1 to 2 patients with transient parasthesia in the foot. Based on the neuro-anatomy, these transient neural paresthesias were assessed to be entirely based on pressure from positioning in stirrups around the ankle and not related to the sling or sling procedure. Otherwise, in our 20 years of experience, we have not encountered neurologic complications.

Regarding chronic pain, we have not encountered any chronic pain in our TVT, TVT-O, TVT Exact or TVT Abbrevo procedures. We have surgically revised patients with chronic pain after various slings. The usual finding is that the sling is too tight and needs to be released, or that the healing process was accompanied by muscle spasm of the pelvic floor, exacerbating a problem of pre-existing pelvic pain or initiating pain on a muscle spasm basis. Pelvic physical therapy and myofascial release are often helpful to resolve symptoms. We are readily able to resolve the rare incidence of pain issues related to TVT procedures.

E. Risks of Surgical Alternatives to Midurethral Slings

No surgical alternative to TVT, TVT-O, TVT Exact or TVT Abbrevo avoids the risks of mesh midurethral slings.

Ward and Hilton's comparison of long-term outcomes of TVT and Burch colposuspension did not detect a significant differencc between the procedures for cure of SUI at five years. Cure of SUI and improvement in QOL were maintained over the long term. However, vault and posterior vaginal wall prolapse were seen more commonly after colposuspension and mesh erosion could occur several years after surgery. Complications after both procedures included pain with intercourse and LUTS, (Ward, KL, Hilton, P, Tension-free

vaginal tape versus colposuspension for primary urodynamic stress incontinence: 5-year follow up, Br J Obstet Gynecol, 226-233, 2007.)

Albo and colleagues randomly assigned 655 women to Burch (329) or autologous fascial sling (326). 79%, or 520 women, completed the outcome assessment. At 24 months, the overall success rate was 47% for sling and 38% for Burch and success specific to stress incontinence was 66% for sling and 49% for Burch. UTIs, difficulty voiding and postoperative urge were also higher in the autologous fascial sling group, however. Other adverse events reported were ureteral injury (Burch group but not sling group); ureterovaginal fistula (Burch group but not sling group); incidental vaginotomy (Burch group but not sling group); incidental cystotomy (10 in Burch group, 2 in sling group); erosion of suture into bladder (1 in Burch group, 0 in sling group); recurrent cystitis (5 in Burch group, 6 in sling group); pyelonephritis (1 in Burch group, 1 in sling group); catheter complication (1 in Burch group, 1 in sling group); voiding dysfunction leading to surgical revision (0 in Burch group, 20 in sling group); pelvic pain (0 in Burch group, 2 in sling group); bleeding (3 in Burch group, 1 in sling group); and wound complication requiring surgical intervention (13 in Burch group, 11 in sling group). (Albo 2007.)

Schimpf's metaanalysis noted incidence of complications of Burch and pubovaginal (including autologous fascial) sling including transfusion, hematoma, dyspareunia (pubovaginal only) return to operating room for erosion, exposure, wound infection, UTI, bowel injury (Burch only), ureteral injury, OAB, urinary retention (lasting less than and also greater than six weeks postoperatively), return to operating room for urinary retention, groin pain, bladder perforation, urethral perforation (Burch only), vaginal perforation, deep vein thrombosis. In comparing MUS vs. Burch, the authors recommended either intervention. In comparing pubovaginal sling v. Burch, the authors recommended pubovaginal sling to maximize cure outcomes. In comparing

obturator vs. retropubic MUS, the authors recommended either for cure outcomes and that the decision should balance adverse events. (Schimpf 2014.)

F. Evidence from the Peer-Reviewed Scientific Literature

My opinions on TVT, TVT-O, TVT Exact and TVT Abbrevo are based upon the highest quality of evidence, in that they are based primarily on meta-analyses and systematic reviews of the peer-reviewed medical literature. They also are based on my experience as a practitioner, my training as a FPMRS Board certified urogynecologist, my professional education, my review of the peer-reviewed medical literature more broadly, my conversations with my colleagues and my medical school education. Systematic reviews and meta-analyses provide the highest levels of scientific evidence. Meta-analyses are "studies of studies" that extract and combine data to produce a summary result. Meta-analysis is the statistical analysis of a large collection of results from individual studies for the purpose of integrating the findings. Systematic reviews use explicit and reproducible methods to systematically search, critically appraise and synthesize the results of multiple primary studies and thereby reduce biases and random errors. The plaintiffs in this litigation, by contrast, have based their theories on the lowest quality of evidence such as case series, case reports and unsupported expert opinions. Midurethral sling operations are the most extensively researched surgical treatment for SUI in women in history. The highest quality of medical evidence demonstrates that midurethral slings such as TVT, TVT-O, TVT Exact and TVT Abbrevo are effective, safe and improve women's quality of life. (Schimpf 2014; Ford 2015.)

i. TVT

The 2015 Ford Cochrane Systematic Review of midurethral sling operations for SUI in women analyzed large registries on retropubic MUS, most of which slings were TVT, and found low rates of major complications. The number of procedures reported in the registries ranged from 809 to 4281. Bladder perforations occurred in 2.7% to 3.9% of cases; reoperation rates related to MUS insertion or postoperative voiding dysfunction ranged from 1.6% to 2.4%; urinary retention rate was 1.6%; pelvic hematoma occurred in 0.7% to 1.9% of women; infection rate was 0.7%; erosion/extrusion rate was 1.5% and groin pain occurred in 0.4% of women. Ford and colleagues noted that these complication rates were similar to those reported in the trials included in their systematic review, which included 81 trials that evaluated 12,113 women. Ford and colleagues concluded that midurethral slings, which include TVT and TVT Exact, are widely accepted as a routine surgical treatment for SUI; that they are highly effective in the short and medium term, with mounting evidence demonstrating their effectiveness in the long term; and that they significantly improved women's outcomes for quality of life and sexual function. (Ford 2015.)

The recent 2017 Cochrane systematic review by Ford and colleagues supported these same conclusions and findings and noted that we now have eighteen years' worth of data since the initial report of the retropubic TVT. (Ford, et al, Mid-urethral sling operations for stress urinary incontinence in women, Cochrane Database of Systematic Reviews 2017, Iss. 7, Art. No.: CD006375. DO: 10.1002/14651858.CD006375.pub4.) The Cochrane Reviews of 2015 and 2017 consist of the highest level of scientific evidence and they expand upon earlier Cochrane Reviews on midurethral slings published during the decade prior.

Schimpf and colleagues conducted a systematic review of peer-reviewed randomized controlled trials that compared at least two sling procedures (including autologous slings), or a sling procedure to Burch, with at least 12 months of follow-up. Included in the review were comparisons of MUS to Burch, of autologous pubovaginal slings to Burch, of pubovaginal slings to MUS, of retropubic MUS to obturator MUS, and others. For the purpose of evaluating adverse events, the analysis also included trials excluded from their RCT analysis, as well as nonrandomized comparative studies and cohort studies of any follow-up duration. TVT was overwhelmingly the retropubic MUS most used in the randomized controlled trials that were analyzed. The authors noted that MUS have become more common than pubovaginal sling procedures and Burch; that their analysis supports the use of MUS over pubovaginal slings; that pubovaginal sling is more effective than Burch; and that no difference in effectiveness was found between retropubic and obturator route MUS, and therefore the approach chosen may be based on risks associated with each. The authors specifically noted that TVT is the best studied surgical procedure for SUI. (Schimpf 2014.)

Novara et al. performed a systematic review of 169 studies, 33 of which were randomized controlled trials. Novara noted that TVT and other midurethral slings had gained large popularity since their launch due to the ease of the procedure and its effectiveness and because complications were low. The authors concluded from their meta-analysis that complication rates were similar after TVT and Burch, although bladder perforations were more common after TVT and reoperation rates were significantly higher after Burch. TVT and pubovaginal slings were followed by similar complication rates, although there was limited data comparing efficacy of TVT to autologous slings. A 2007 meta-analysis by Novara determined that TVT specifically had outperformed Burch procedures and other retropubic slings for continence rates. (Novara, et

al, Complication rates of tension-free midurethral slings in the treatment of female stress urinary incontinence: A systematic review and meta-analysis of randomized controlled trials comparing tension-free midurethral tapes to other surgical procedures and different devices, Eur Urology 2008, 53:288-209; Novara, et al, Tension-free midurethral slings in the treatment of female stress urinary incontinence: A systematic review and meta-analysis of randomized controlled trials of effectiveness, Eur Urology 2007, 52: 663-679.)

Tomaselli et al conducted a systematic review and meta-analysis of 11 RCTs and 38 nonrandomized studies of a total of 6,406 patients to evaluate the long-term effectiveness and safety of retropubic MUS (as well as the medium-term results for obturator MUS). TVT was implanted in 5 of the 11 RCTs and in 25 of 38 nonrandomized studies, and 3,801 of the 6,406 patients were implanted with TVT. The meta-analysis showed that retropubic MUS are associated with high objective and subjective cure rates in the long-term and medium term. Only 13 of 3,974 patients implanted with a retropubic MUS reported persistent or chronic pain, defined as pain persisting beyond the perioperative period or reported at the last post-operative visit. Only 55 of those 3,974 patients reported persistent or severe voiding problems. The authors concluded that the efficacy of retropubic MUS was backed by a high safety profile and by a limited number of complications that were seldom severe. They noted that a number of meta-analyses evaluating MUS have shown both their superiority in comparison with Burch colposuspension and autologous fascia slings and their efficacy and safety in different patient populations, referencing systematic reviews and meta-analyses by Novara, Latthe, Ogah, Mostafa, Agur, Zhu, Madhuvrata, Tan, Tan and Schimpf. (Tommaselli, et al, Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: A systematic review and meta-analysis, Int Urogynecol J 2015 Sep, 26(9): 1253-68.)

Referencing systematic reviews by Novara, Schimpf, Dean and Rehman, Nager shows how the highest level of scientific evidence favors MUS, as a minimally invasive procedure, over non-mesh SUI surgeries in terms of less blood loss, less operative time, fewer hospital stays, fewer hematomas and fewer wound infections. (Nager 2016.)

ii. TVT Exact

TVT Exact has efficacy and safety outcomes equivalent to TVT, as has been reported in the peer-reviewed scientific literature, and as I have seen in my own practice, having implanted several hundred TVTs as well as TVT Exacts. Anderson reported subjective success rates of 92 to100% and low complication rates after implanting 133 TVT Exacts (and 8 other MUS) in 75 women who demonstrated Valsalva voiding and 66 women who did not. (Anderson, et al, Safety and efficacy of retro pubic mid-urethral sling placement in women who void with Valsalva, Female Urology, Urodynamics, Incontinence, and Pelvic Floor Reconstructive Surgery 2016, 52-57.) Bezhenar reported a 98.3% success rate and 1.1% to 5.6% incidence of postoperative complications with TVT Exact, TVT and two obturator-route MUS. (Bezhenar, et al, 7-Year Old Clinical Experience of Treating Women's Urinary Incontinence Using Suburethral Slings, D. O. Ott's Research Institute of Obstetrics and Gynecology, NWD RAMS 768.) Thubert showed that the success rate of TVT Exact and TVT was similar at 12 months follow up, and that although the prevalence of bladder injury was unchanged with TVT Exact compared with TVT, post-operative pain was decreased. (Thubert et al, Bladder injury and success rates following retropubic mid-urethral sling: TVT Exact vs. TVT, Eur J Obstet Gynecol, 198:78-83, 2016.)

Sun and colleagues noted that TVT Exact and TVT Abbrevo had built on the success of TVT and TVT-O when comparing the efficacy of TVT Exact and TVT Abbrevo in normal vs.

overweight women. They found that in the normal weight patients, the subjective and objective cure rates were high for both TVT Abbrevo and TVT Exact (objective rates of 94.12% and 95.61% respectively and subjective results of 92.44% and 94.74% respectively.) In overweight patients, the objective cure rates were better for TVT Exact patients than TVT Abbrevo patients (95.65 vs. 76.24, respectively), as were the subjective cure rates (vs. ,respectively), leading the authors to conclude that while there were no significant differences in the rate of subjective or objective efficiency between the different procedures in normal weight patients, TVT Exact may be more effective for overweight patients than TVT Abbrevo. The authors noted that possible complications of the slings include major vascular injury, retropubic hematoma, major visceral injury, bladder injuries and postoperative voiding dysfunction. (Sun, Y., et al., The Efficiency and Safety of Tension-Free Vaginal Tape (TVT) Abbrevo Procedure Versus TVT Exact in the Normal Weight and Overweight Patients Affected by Stress Urinary Incontinence, Urology, 110:63-69, 2017.)

Marschke and colleagues compared TVT Exact vs. RetroArc, another manufacturer's sling, in a prospective noninferiority RCT in 152 (Exact) and 151 (RetroArc) women. The authors determined that at 3 and 12 months, RetroArc was not inferior to TVT, but with regard to subjective cure, results were significantly better for TVT Exact (76.1% vs. 54.3%). The majority of complications were voiding difficulties and were lower after the TVT Exact. There were no bowel or urethra injuries, or postoperative infections or impaired healing.

iii. TVT Obturator (TVT-O)

The most recent (2017) Cochrane systematic review and meta-analysis of midurethral slings for stress urinary incontinence in women included 55 RCTs (with data on 8,652 women)

comparing transobturator route to retropubic route. Ford and colleagues concluded that transobturator midurethral slings, like retropubic midurethral slings, "are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term." They further concluded that both slings have a "positive impact on improving the quality of life of women with SUI"; that fewer adverse events occur with transobturator approach slings compared with retropubic slings, with the exception of groin pain; and that three studies suggest that transobturator slings may be more cost-effective. Ford et al noted that there is some limited evidence that obturator route slings result in a higher reoperation rate, but that both obturator route and retropubic route slings have a 2% rate of exposure. Finally, the authors concluded that rates of problems with sexual intercourse after obturator as well as retropubic slings, including pain, are low. (Ford 2017.)

Based on their meta-analysis of 21 RCTs comparing retropubic vs. obturator slings, Schimpf and colleagues (for the Society of Gynecologic Surgeons Systematic Review Group) recommended either retropubic or obturator approach midurethral slings for objective and subjective cure outcomes. Quality-of-life and sexual function outcomes were also similar between the 2 procedures. Schimpf et al recommended that the decision as to obturator or retropubic approach balance adverse events and be based on which adverse events are of most concern to the patient. While retropubic slings result in lower rates of sling erosion, need to return to operating room for treatment of sling erosion, groin/leg pain, and vaginal perforation, transobturator midurethral slings result in shorter operative time, fewer bladder/urethral perforations, less perioperative pain, fewer urinary tract infections, and less overactive bladder symptoms. (Schimpf 2014.)

Laurikainen and colleagues concluded based on five-year data from their RCT of 268 women randomized to transobturator vs. retropubic midurethral slings that both objective and subjective cure rates for both approaches exceeded 80% even when patients lost to follow up were considered failures. Complication rates were low, with no difference between the groups. No late onset adverse events of the mesh material were seen. No woman had any sign of tissue reaction, erosion, or tape protrusion at five-year follow-up. Patient satisfaction, assessed by condition-specific quality-of-life questionnaires was high, with 88.6% of TVT-O patients and 92.6% of TVT patients stating that they would recommend the procedure to a friend. Subjective treatment satisfaction was 94.2% in the TVT group and 91.7% in the TVT-O group, with no difference between groups. (Laurikainen 2014.)

Cheng and colleagues' prospective study assessing TVT-O in 103 patients found that TVT-O is safe and effective. Complete disappearance of SUI occurred in 87.4% of patients, while improvement was found in about 92%. There was no difference in the cure rate between year 1 and year 5. In 90 patients, frequency and urge symptoms were significantly improved five years after the procedure. 17.4% needed catheterization for a period of time after the procedure. For those who continued with obstructive symptoms and postvoid residual at one year after TVT-O, the severity of these symptoms at five years after were not improved compared with one year after. Within the first 6 months, the most prevalent complaint was groin pain, which was observed in 25 patients (24.3%). At one-year follow-up, only four patients (3.8%) complained of this discomfort. (Cheng, D, Liu, C, Tension-free vaginal tape obturator in the treatment of stress urinary incontinence: a prospective study with five-year follow up, Eur J Obstet Gynecol Reprod Biol, 161:228-232, 2012.)

The five-year follow up of the TOMUS trial assessed 5-year treatment success, satisfaction, symptom specific distress, QOL and adverse events in 404 women from the original equivalence trial in which women were randomized to retropubic or obturator approach slings. The authors found that although treatment success decreased over five years, satisfaction remained high in both groups; and that women undergoing a transobturator sling procedure reported more sustained improvement in urinary symptoms and sexual function. Although new mesh erosions occurred in both groups over time, they did so at a similarly low rate. The authors noted that failure rates for most SUI surgeries increase over time. (Kenton, K, et al, J Urol, 193:203-2010, 2015.)

In the years since the above-referenced and other studies were published demonstrating the favorable risk/benefit profile of TVT-O, the peer-reviewed medical literature has continued to demonstrate long-term efficacy and safety of TVT-O.

Serati and colleagues' ten-year follow up of their multicenter, prospective study of the safety and efficacy of TVT-O (160 of 168 patients available for follow up) showed that TVT-O is a highly effective and safe option for the treatment of SUI. At 10 years after surgery, 155 of 160 patients (97%) declared themselves cured. Similarly, at 10 years follow up, 148 of 160 patients (92%) were objectively cured. No significant deterioration of objective cure rates was observed over time. A history of failure of previous anti-incontinence procedures was the only predictor of recurrent SUI. The onset of de novo overactive bladder was reported by 23 of 160 patients (14%) at 10-year follow-up. No other late complications were reported. (Serati, M, et al, Tension-free Vaginal Tape–Obturator for Treatment of Pure Urodynamic Stress Urinary Incontinence: Efficacy and of patientAdverse Effects at 10-year Follow-up, Eur Urology, 17:674-679, 2017.)

Serdinsek and colleagues performed a ten-year follow up of their RCT comparing TVT-O with Monarc (outside-in) transobturator sling and found objective cure rate for TVT-O of 94.6%, subjective cure rate of 68.3%, and satisfaction rate of 78.7%. There were no cases of mesh exposure. 6.4% of all patients (both Monarc and TVT-O) reported dyspareunia (10.3% of sexually active patients); the authors opined that the dyspareunia might be due to procedure-unrelated causes such as osteomuscular pain, pelvic organ prolapse or vaginal atrophy after menopause. 34% of participants reported LUTS, and the authors emphasized that because of the higher incidence of voiding disorders after menopause, it is possible that de novo LUTS symptoms occurring so late after the procedure could be a natural course of ageing rather than the consequence of MUS procedures. (Serdinsek, T, et al, Long-term results of two different transobturator techniques for surgical treatment of women with stress and mixed urinary incontinence: a 10-year randomized controlled study follow-up, Int Urogynecol J, 30:257–263, 2019.)

Karmarkar and colleagues found a 71.6% patient-reported success rate at nine years' follow up of 341 women randomized to receive either inside-out TVT-O or outside-in TOT-ARIS. An additional 14% of patients reported themselves to be "improved." The patient-reported success rate had declined from 80% at 1 year to 71.6% at 3 years. The authors also found that after three years, the success rate is almost stable, in that there was a clinically insignificant difference between success rates at 3 years and 9 years. A total of 7.96% underwent further continence surgery; the mesh extrusion/erosion rate was 4.5%; and groin pain/discomfort was reported in 4.32% of women, with only 1.4% requiring treatment. 171 patients completed a questionnaire assessing QoL and 87 patients completed the PISQ questionnaire assessing sexual function. Clinically significant improvement in QoL was seen in

76.8%, with no evidence of significant differences between TVT-O and TOT-ARIS. The sexual function score on PISQ-12 showed improvement in 61% and deterioration in 34.5%, with no evidence of any significant difference between TVT-O and TOT-ARIS. (Karmarkar, D, et al, Long-term outcomes of transobturator tapes in women with stress urinary incontinence: E-TOT randomized controlled trial, Br J Obstet Gynecol, 973-981, 2017.)

iv. TVT Abbrevo

TVT Abbrevo has been shown in the peer-reviewed medical literature to be safe and efficacious. The mesh material in TVT Abbrevo is the same mesh material in TVT, TVT-O and TVT Exact (TVT Abbrevo IFU ©2009) and the set of risks of TVT Abbrevo are the same set as for other mesh midurethral slings.

Tommaselli performed a retrospective evaluation of 205 women (105 normal weight, 100 overweight) at 12 months after implantation of TVT Abbrevo. Primary outcomes were objective cure rate and subjective cure rate, and secondary outcomes were intra-operative and post-operative complications. Objective cure rates were 96.2% and 94% respectively in normal-weight and overweight patients. Subjective cure rates in each group were 90.5% and 88% respectively. No serious intra- or post-operative complications were observed. No differences were observed in pain VAS scores and number of analgesic vials administered. Tommasselli et al concluded that TVT Abbrevo seems to have similar efficacy and safety in normal weight and overweight women. (Tommasselli et al, Efficacy and safety of the trans-obturator TVT-Abbrevo device in normal weight compared to overweight patients affected by stress urinary incontinence, Eur J Obstet Gynecol, 197:116-119, 2016.) A prior abstract by Tommaselli concluded that both TVT-O and TVT Abbrevo seem to be effective and safe for the surgical management of SUI and that TVT Abbrevo is associated with less postoperative pain. (Tommaselli, GA, et al, 0692

Comparison of TVT-O and TVT Abbrevo for the Surgical Management of Female Stress Urinary Incontinence: A 12-Months Preliminary Study (Abstract), Int J Gynecol Obstet 119S3: S504, 2012.)

High cure rates and low complications after TVT Abbrevo have been elsewhere reported in the peer reviewed medical literature as well. (Riachi, L., et al., A New Minimally Invasive Treatment Option for Stress Urinary Incontinence in Women: TVT Abbrevo, a Shorter Sling with an Inside-out Transobturator Approach, Gynecology: Surgical Technology International XXIII, 176-180, 2013; Capobioanco, G., et al., TVT: Abbrevo: Efficacy and two years follow-up for the treatment of stress urinary incontinence, Clin. Exp. Obst. & Gyn., XLI, n.4, 445-447, 2014; Canel, V., et al., Postoperative groin pain and success rates following transobturator midurethral sling placement: TVT Abbrevo system versus TVT Obturator system, Int Urogynecol J, 26:1509-1516, 2015; Ragavan, M., TVT Abbrevo – a retrospective cohort of 50 cases between September 2012 and August 2014, BJOG An International J of Obstet Gynaecol, 339, 2015; Kurien, A., et al, TVT abbrevo for management of female stress urinary incontinence: a prospective analysis over 22 months in a tertiary care hospital (Abstract), Br J Obstet Gynecol, 121(2):234-235, 2014.)

Potential complications of TVT Abbrevo/transobturator route slings noted in the peer-reviewed medical literature on TVT Abbrevo include de novo overactive bladder (Capobianco, 1.78%) and continued overactive bladder (3.57%); vaginal injury, post-operative voiding problems, UTIs and de novo urgency (Tommaselli 2015); pain (Tommasselli 2012); immediate and persistent groin pain, unilateral or bilaterial pain, thigh, hip, lumbar spine and sciatalgia pain, and dyspareunia (Riachi). The TVT Abbrevo IFU includes the risks of punctures or lacerations of vessels, nerves, bladder, urethra or bowel; transitory local irritation at the wound site;

extrusion, erosion, fistula formation or inflammation; potentiation of an existing infection; over-correction causing temporary or permanent lower urinary tract obstruction; bleeding; bladder injury; recurren incontinence; dysuria; transient leg pain; de novo detrusor instability; mechanical damage to the mesh if the mesh comes into contact with staples, clips or clamps.

G. The Gold Standard

As noted above, MUS are the best studied surgical procedures for SUI, and TVT in particular is the most studied MUS. Although non-mesh SUI surgeries including Burch procedures and autologous fascial sling surgeries have existed for decades, there is relatively little data on these procedures. The highest level of scientific evidence available favors MUS, including TVT, TVT-O, TVT Exact and TVT Abbrevo, over Burch and pubovaginal slings. MUS are the gold standard for surgical treatment of SUI. As a result, MUS slings including TVT, TVT-O, TVT Exact and TVT Abbrevo are taught in medical residencies and fellowships. As stated above, I have trained 225 residents and 10 fellows on how to implant midurethral slings.

The major urogynecological and urological professional medical societies, including those that I am a member of, AUGS and ACOG, have published position statements or practice bulletins in support of the use of MUS as a primary surgical treatment for SUI.

The American Urogynecologic Society (AUGS) and the American Congress of Obstetricians and Gynecologists (ACOG) published Practice Bulletin No. 155, Urinary Incontinence in Women, in November 2015. AUGS and ACOG stated in this Bulletin that synthetic midurethral mesh slings are the most common primary surgical treatment for SUI in women; that they demonstrate efficacy that is similar to non-mesh surgeries but with fewer

adverse events than fascial slings and less voiding dysfunction than Burch colposuspensions. For these reasons, AUGS and ACOG noted, MUS have become the primary treatment for SUI in women, and there are substantial safety and efficacy data that support the role of MUS as a primary surgical treatment option for SUI in women.

AUGS and the Society for Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) published a Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence in January 2014, and then an updated statement in June 2016 and a further updated statement in February 2018, in support of the use of the midurethral sling in the surgical management of SUI. In the Statement, which was also supported by the American Association of Gynecological Laparoscopists (AAGL), ACOG, the National Association for Continence (NAFC), the Society of Gynecological Surgeons (SGS), the International Urogynecological Association (IUGA), AUGS and SUFU stated that polypropylene material is safe and effective as a surgical implant; that the monofilament polypropylene mesh MUS is the most extensively studied anti-incontinence procedure in history; that polypropylene mesh midurethral slings are a standard of care for the surgical treatment of SUI and represent a great advance in the treatment of this condition for our patients; and that the FDA has clearly stated that the polypropylene MUS is safe and effective in the treatment of SUI. In conclusion, AUGS and SUFU stated:

> The polypropylene midurethral sling has helped millions of women with SUI regain control of their lives by undergoing a simple outpatient procedure that allows them to return to daily life very quickly. With its acknowledged safety and efficacy, it has created an environment for a much larger number of women to have access to treatment. In the past, concerns over failure and invasiveness of surgery caused a substantial percentage of incontinent women to live without treatment. One of the unintended consequences of this polypropylene mesh controversy has been to keep women from receiving any treatment for SUI. This procedure is probably the most important advancement in the treatment of stress urinary

> incontinence in the last 50 years and has the full support of our organizations which are dedicated to improving the lives of women with urinary incontinence.

In the position statement, the American Associationof Gynecological Laparoscopists (AAGL)(7,600 members), the American Congress of Obstetricians and Gynecologists (ACOG)(57,000 members), the American Urogynecologic Society (AUGS)(1,700 members), the International Urogynecological Association (IUGA)(3,000 members), the Society for Gynecologic Surgeons (SGS) and the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU)(500 members), reaffirmed their collective support for the use of midurethral slings, including synthetic polypropylene slings, for the surgical treatment of SUI.

H. IFUs and Patient Brochures

The Instructions for Use (IFU) of the TVT, TVT-O, TVT Exact and TVT Abbrevo appropriately warn of the risks associated with these devices. Again, the risks of these devices are commonly known to experienced pelvic surgeons, who are knowledgeable of the risks from medical school, residency and post-residency training, professional education, discussions with their colleagues, review of the peer-reviewed medical literature and their own practice.

I am aware that labeling for prescription medical devices is not required by the FDA to include contraindications, side effects, precautions and hazards if that information is commonly known to the practitioners who use the device. 21 CFR 801.109(c). An FDA document entitled Device Labeling Guidance Number G91 – 1 clearly indicates that a device is misbranded if the labeling does not bear:… information for use including… any relevant hazards, side effects, and precautions… (Page 6 to 7). The document goes on to describe what must be included in what may be omitted. It states "such information may be omitted from the dispensing package if but only if directions, hazards, warnings, and other information are commonly known to

practitioners licensed by law to use the device." While I have considered these in formulating my opinions in this report on the adequacy of the IFUs, my opinions are most heavily based on my experience, training, education and review of the medical literature.

The IFUs do not contain, and need not contain, every possible risk of TVT/TVT-O/TVT Exact. The risks, as discussed in this report, are commonly known to experienced pelvic floor surgeons as a result of the surgeons' education and training, professional experience, discussion with peers at medical society conferences, and review of the medical literature.

The IFUs include numerous medical complications which have pain as an indisputable component or symptom. For example: infection, erosion and fistula are all known to cause pelvic pain. Puncture or injury of a nerve, blood vessel, or organ are universally understood to be serious complications with risk of pain and risk of death, and they are cited as risks in the IFU. Inflammation, which is also listed in the IFU, is also universally known to be a complication which has pain as principle characteristic. The IFUs therefore include warnings that go far beyond pain as an isolated concern. Many conditions which indisputably cause pain are included and several risks which can be life threatening are included within the IFU. The IFU therefore provides information for physicians which informs them in multiple ways of risks of pain.

By way of an analogy, the Futura safety scalpel IFU (Futura : Merit Medical Systems, INC South Jordan, Utah) describes steps for proper usage and specifies that "used sharps are contaminated, handle carefully…." It does not include the risk of infection, but any surgeon understands that if s/he were cut by a used scalpel s/he could develop an infection even though "infection" is not included as an adverse event. Nor would the IFU be inadequate because it did not include the risk of pain. Surgeons understand that if cut by a knife there will be pain.

In orthopedic surgery, synthetic knee implants are a common procedure. The Klassic Knee System by Total Joints Orthopedics, Salt Lake City, Utah IFU Adverse Effects section reads in its entirety:

ADVERSE EFFECTS The following adverse effects have been reported for total knee replacement:

- Corrosion of metal implants
- Deep wound infections
- Disassembly of modular components
- Dislocation and subluxation
- Early or late loosening of components
- Malalignment of the prosthetic knee components
- Fatigue fracture
- Venous thromboembolic disease
- Inflammatory reactions or osteolysis
- Metal sensitivity
- Peripheral neuropathies or subclinical nerve damage
- Tissue or allergic reaction to corrosion, wear, or cement particles

This list has many serious complications. Corrosion is similar to erosion (and has long been recognized as a risk of metal implants, Williams, D., Corrosion of Implant Materials, Annu Rev Mater Sci, 6:237-266, 1976). Dislocation of the device (which means the implant holding the upper leg and lower leg together become dislodged), venous thromboembolism and

osteolysis (which mean the destruction of disappearance of bone tissue) are very serious risks. All of these adverse events, along with infection, inflammation and nerve injury, which are also listed, can cause pain, but the word "pain" is not in the IFU because pain is understood by surgeons—the users of IFUs—to be a consequence of the listed adverse events.

The IFU does not need to bridge the gap between the adverse events and symptoms that qualified surgeons know are associated with the listed adverse events. It is commonly known to gynecologic surgeons that inflammation, perforation of a nerve, perforation of an organ, fistula formation, erosion, extrusion and scarring are all commonly associated with pain.

Similarly, pain and dyspareunia, whether short term or long term, with all vaginal surgery, was common knowledge for pelvic surgeons at the time that TVT, TVT-O, TVT Exact and TVT Abbrevo became available, as further described herein. (Francis, WJA, Jeffcoate, TNA, Dyspareunia following vaginal operations, J Obstet Gynaecol Br Commonweal, 68(1):1-10, Feb 1961; Haase, Skibsted, Influence of operations for stress incontinence and/or genital descensus on sexual life, Acta Obstet Gynecol Scand 67: 659 - 661, 1988; Kahn, M., Stanton, S., Posterior colporrhaphy: Its effects on bowel and sexual function, Br J Obstet Gynecol, 104:82-86, 1997; Weber 2000; Barksdale, PA, et al, Intraligamentous Nerves as a Potential Source of Pain After Sacrospinous Ligament Fixation of the Vaginal Apex, Int Urogynecol J, 8:121-125, 1997.)

Dyspareunia after use of mesh in gynecological surgeries was reported in the peer-reviewed medical literature prior to TVT. (Iglesia 1997.) Moreover, it is commonly known to surgeons across non gynecologic specialties that chronic pain is a risk of any surgery. (Kalkman, CJ, et al, Preoperative prediction of severe postoperative pain, Pain 105:415-423, 2003; Kehlet, H., et al, Persistent postsurgical pain: risk factors and prevention, Lancet , 367: 1618–25, 2006;

Crombie, IK, et al, Cut and thrust: antecedent surgery and trauma among patients attending a chronic pain clinic, Pain, 76:167-171, 1998; Reuben, SS, Preventing the Development of Complex Regional Pain Syndrome after Surgery, Anesthesiology 101:1215–24, 2004.)

For every surgeon there is baseline training and experience, education, review of available research, and other sources of information with together are the information amalgam each surgeon uses to make decisions and to give informed consent. There is no one single document which is the 'be-all and end-all" document upon which all decisions are based. The TVT, TVT-O and TVT Abbrevo IFUs are one source of available information, and they would not be expected to be the sole source of information in preparation to use the product. It is not the principle and sole information document surgeons rely on in a decision to use the device. A half century of research and available information demonstrates that pain at the implantation site of an implant and the possible need to remove an implant were established risks in the scientific literature, educational meetings, peer to peer communication, among other sources.

The IFUs note that they are not a comprehensive reference to surgical technique for correcting SUI and that the device should be used only by physicians trained in the surgical treatment of Stress Urinary Incontinence and specifically in implanting the TVT device.

Literature supports the contention that an IFU is not the primary and solitary source of information used in evaluating a procedure or product. Kirkpatrick and colleagues found by surveying 314 members of the American Urological Association that 64.4% of respondents reported they had never read the IFU before mesh placement for prolapse. The authors noted that the large percentage of surgeons who had not read the IFU suggests that, "the IFU is neither a decisive factor in the decision making process regarding mesh implantation nor the sole tool for conveying risks and warnings for many surgeons." (Kirkpatrick, G., et al., Transvaginal

Mesh Placement and the Instructions for Use: A Survey of North American Urologists, Urology Practice, 6:135-139, Mar 2019.)

In addition, the TVT, TVT-O, TVT Exact and TVT Abbrevo patient brochures urge patients repeatedly to discuss treatment options and the risks and benefits of midurethral slings with their doctor. The patient brochures do not replace the surgeon's obligation to have a robust informed consent process with their patients regarding risks and benefits of and alternatives to TVT slings. The patient brochures were adequate to advise patients of risks of the midurethral slings in conjunction with advising patients to discuss the risks and benefits of MUS with their doctor.

Ethicon's other professional education content also appropriately warns of the risks associated with TVT, TVT-O, TVT Exact and TVT Abbrevo. These include the TVT Surgeon's Resource Monograph, surgical videos, anatomy animations, and professional education events such as cadaver labs, didactics, proctorships and preceptorships. Ethicon's professional education content is appropriate in that it includes risks of the devices reported in the peer-reviewed medical literature and experienced by surgeons.

I. Response to Plaintiffs' Themes

i. Biocompatibility of Prolene Mesh

The plaintiffs in this litigation claim that the mesh in TVT, TVT-O, TVT Exact and TVT Abbrevo is "heavyweight" mesh and that the pore size of the mesh is too small. However, the mesh in TVT, TVT-O, TVT Exact and TVT Abbrevo, Prolene, is macroporous, monofilament type I mesh, which the scientifically literature has shown is inert, resists infection and fistula, has

rapid fibrinous fixation, becomes completely incorporated into the host tissue, and in case of infection does not need to be removed.

Prolene has a pore size of 1,379 microns. Macroporous monofilament polypropylene mesh with a pore size that are larger than 75 microns and does not promote or harbor infection, and mesh with pore size larger than 100 microns produces complete infiltration of the host tissue into the entire thickness of the mesh in about one month. The mesh in TVT, TVT-O, TVT Exact and TVT Abbrevo has also been scientifically demonstrated to have low stiffness. (Amid 1997; Dietz 2003; Moalli, et al, Tensile properties of five commonly used mid-urethral slings relative to the TVT, Int Urogynecol J 2008, 19:655-63.)

ii. Cytotoxicity, Degradation and Particle Shedding

The plaintiffs in this litigation claim that the mesh in TVT, TVT-O, TVT Exact and TVT Abbrevo is cytotoxic, degrades, sheds particles and cracks. There is no peer-reviewed scientific literature that proves their claims, and I have never seen evidence in my practice that patients are harmed by the mesh in TVT, TVT-O, TVT Exact and TVT Abbrevo being cytotoxic, degrading, shedding particles or cracking. In a 2010 article, Clave and colleagues analyzed 100 polypropylene and polyethylene terephthalate implants explanted from patients with complications, and observed what appeared to be microscopic cracking and degradation of the samples. These observations led the authors to question whether polypropylene mesh is truly inert. The authors acknowledged that their study did not provide the opportunity to analyze implants from non-pathological situations; that their sample size was small; that they had not performed a full chemical analysis of every sample; and that they were unable to explain their observations. (Clave, et al, Polypropylene as a reinforcement in pelvic surgery is not inert:

comparative analysis of 100 explants, Int Urogynecol J (2010) 21:261-270.) Thames and colleagues, however, subsequently published the results of a study they performed of explanted Prolene meshes that had been cleaned from which they concluded that Prolene mesh did not degrade in vivo, that properly formulated polypropylene was stable in vivo, and that the cracked layer identified by other researches was instead an adsorbed protein-formaldehyde coating that resulted from the formalin-protein-fixation process, which occurs immediately upon placing an explant in formalin. (Ong, et al, The myth: in vivo degradation of polypropylene meshes, Int Urogyn J 2016, 27:s37-8; Thames, et al, The myth: in vivo degradation of polypropylene meshes, Int Urogynecol J, 2017 Feb, 28(2):285-97.) Thames and colleagues' findings are consistent with the large body of peer-reviewed medical literature, as well as what I have seen in my practice. No peer-reviewed scientific literature has demonstrated that patients have been harmed by degradation of, cracking of or particle loss from the mesh in TVT, TVT-O, TVT Exact and TVT Abbrevo. Other microscopic analyses of macroporous monofilament polypropylene mesh that were removed for reasons other than an infection process are consistent with Thames's findings, and the investigators there concluded that no degradation of polypropylene mesh had occurred. (Fletcher SG and Lemack GE: Re: Histologic comparison of pubovaginal sling graft materials: a comparative study. Urology 2008; 72: 721; Woodruff AJ, Cole EE, Dmochowski RR et al: Histologic comparison of pubovaginal sling graft materials: a comparative study. Urology 2008; 72: 85). Ethicon has The FDA has specifically recognized that the biocompatibility of Prolene has been established [53 Fed. Reg. 23856 (June 24, 1988)]

iii. Infection, Bacterial Slime and Biofilm

The plaintiffs claim that the mesh in TVT, TVT-O, TVT Exact and TVT Abbrevo is prone to infection and promotes bacterial slime and biofilm that harms patients. There is no peer-reviewed scientific literature that supports their claims. Macroporous monofilament polypropylene mesh is a Type I mesh with pore sizes larger than 75 microns, and therefore does not promote or harbor infection. (Amid 1997.) Infection of the mesh in TVT, TVT-O, TVT Exact and TVT Abbrevo is rare, despite the fact that the vagina is a clean-contaminated environment. Bacteria in the human body are attacked by leukocytes and macrophages and eliminated. (Papadimitriou, Petros: Histological studies of monofilament and multifilament polypropylene mesh implants demonstrate equivalent penetration of macrophages between fibrils, Hernia 2005, 9:75). Infection is a risk of any surgery, however, and the IFU warns that acceptable surgical practice be followed as well as for the management of contaminated or infected wounds, that the mesh may potentiate an existing infection and that infection may require removal of the mesh. As noted above, the FDA has specifically recognized that the biocompatibility of Prolene has been established [53 Fed. Reg. 23856 (June 24, 1988)]

iv. Shrinkage

The plaintiffs claim that the mesh in TVT, TVT-O, TVT Exact and TVT Abbrevo shrinks and contracts, harming patients. As discussed above, shrinkage or contraction of mesh itself has never been demonstrated in the peer-reviewed scientific literature. (Lo 2004; Lukacz 2003; Dietz 2003; Dietz 2011.) Although tissues can contract, this is a phenomenon that was known and reported on in the scientific literature before the advent of TVT (Amid 1997), and it is associated with non-mesh surgeries as well.

v. LCM vs. MCM

The plaintiffs claim alternately that the mesh in TVT, TVT-O, TVT Exact and TVT Abbrevo harms patients either because it is mechanically cut (TVT and TVT-O) or laser-cut (TVT, TVT-O, TVT Exact and TVT Abbrevo). There is no peer-reviewed scientific literature that supports either claims. On the contrary, no studies that have compared results for patients who received a laser-cut MUS vs a mechanically cut MUS have demonstrated any difference in adverse events or efficacy due to whether the MUS was laser cut or mechanically cut. (Neuman, et al, Transobturator vs single-incision suburethral mini-slings for treatment of female stress urinary incontinence: early postoperative pain and 3-year follow-up, J Minim Invasive Gynecol 2011 Nov/Dec, 18(6):769-773; Agarwala, A randomized comparison of two synthetic mid-urethral tension-free slings, UroToday Int J 2008 Oct, 1(4), DOI:10.3834/uij.1939-4810.2008.10.05; Lim, Do the Advantage slings work as well as the tension-free vaginal tapes? Int Urogynecol J 2010, 21:1157-62.) I have used both laser cut and mechanically cut slings in my practice and have never observed any difference in safety or efficacy in my patients depending on whether they have been implanted with a laser-cut sling or a mechanically cut sling.

vi. Cancer

The plaintiffs claim that the mesh in TVT, TVT-O, TVT Exact and TVT Abbrevo causes cancer. However, no reports of malignancy have been reported in humans in association with polypropylene midurethral slings. Tumors related to the implantation of surgical grade polypropylene in humans have never been reported. As Moalli et al wrote, it would be a tragedy for women worldwide if nonscientifically based articles regarding the potential hazards of polypropylene incited a spiraling course for the best surgical procedure developed to date for

stress urinary incontinence. (Moalli, et al, Polypropylene mesh: evidence for lack of carcinogenicity, Int Urogynecol J 2014 March, 25:573-6; King, Goldman, Current controversies regarding oncologic risks associated with polypropylene midurethral slings, Curr Urol Rep 2014, 15:453; Linder, et al, Evaluation of the local carcinogenic potential of mesh used in the treatment of female stress urinary incontinence, Int Urogynecol J 2016 Sep, 27(9):1333-6.)

vii. Vypro, PVDF and Ultrapro

The plaintiffs claim that other meshes, such as Vypro, PVDF and Ultrapro are safer than or superior to the Prolene mesh in TVT, TVT-O, TVT Exact and TVT Abbrevo. However, there is very little data on the use of Vypro, Ultrapro or PVDF in midurethral slings in humans, unlike the voluminous data that exists on the use of macroporous monofilament polypropylene midurethral slings. Reliable conclusions about the safety or efficacy of these materials in midurethral slings simply cannot be drawn based on existing data.

With regard to PVDF, I am not aware of this material being available in the U.S. for gynecological applications or used by any pelvic surgeons in this application. (Okulu E, et al, Use of three types of synthetic mesh material in sling surgery: a prospective randomized clinical trial evaluating effectiveness and complications, Scan J Urol 2013: 47: 217-224; Najjari, et al, Visualization of polypropylene and polyvinylidene fluoride slings in perineal ultrasound and correlation with clinical outcome, BioMed Res Int, 2014, doi:10.1155/2014/181035; Najjari, et al, Comparing different types of suburethral slings using perineal ultrasound, ICS Abs 401, 2012; Goretzlehner, et al, PVDF as an implant material in urogynaecology, Biomaterialien 2007, 8(S1):28-9.)

In response to plaintiffs' assertion that Ultrapro, Vypro and PVDF are better alternatives to Prolene mesh and the TVT, TVT-O, TVT Exact and TVT Abbrevo, this is in reality an

impossible opinion, because these materials are not being taught or used to any significant degree or regularly published on in the scientific literature, unlike Ethicon's TVT slings.

Conclusion

In conclusion, my opinions on the TVT, TVT-O, TVT Exact and TVT Abbrevo, as explained and supported herein, include the following:

- The resounding scientific consensus among urogynecologists and urologists is that type I, macroporous, monofilament, polypropylene midurethral slings, including TVT, TVT-O, TVT Exact and TVT Abbrevo are the gold standard surgical treatment for stress urinary incontinence.
- That these midurethral slings are the gold standard is supported by all of the major professional medical societies in urogynecology, gynecology and female urology.
- The midurethral sling is the single most studied surgery to treat SUI, and its safety and efficacy is supported by the highest levels of scientific evidence.
- The peer reviewed literature overwhelmingly supports, in over 2,000 articles published over 20 years, the use of type I, macroporous, monofilament, polypropylene midurethral slings, including TVT, TVT-O, TVT Exact and TVT Abbrevo.
- The potential complications of these slings comprise the same set of potential complications of alternative anti-incontinence surgeries such as Burch colposuspension and autologous fascial slings, and no alternative SUI surgery eliminates these potential complications.

- Among urogynecologists, gynecologists and urologists, these slings almost have entirely replaced every alternative SUI surgery, for the above reasons.
- Ethicon's IFUs, professional education materials and Surgeon's Resource Monograph appropriately warn surgeons of the risks of these devices, and their patient brochures are appropriate for use by physicians when counseling patients on potential risks and benefits.
- Plaintiffs' experts rely on low-quality articles and case reports while disregarding the overwhelming scientific evidence against their opinions.